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## Attenuated Atrial Natriuretic Peptide-Mediated Lipolysis in Subcutaneous Adipocytes of Obese Type 2 Diabetic Men

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### Abstract

Catecholamines and atrial natriuretic peptide (ANP) are major regulators of adipocyte lipolysis. Although obesity is characterized by catecholamine resistance in subcutaneous adipose tissue (SCAT), data on ANP lipolytic response and sensitivity in different adipose tissue (AT) depots of metabolically distinct humans are scarce. Ex vivo catecholamine- and ANP-induced lipolysis was investigated in adipocytes derived from SCAT and visceral AT (VAT) depot of lean (n=13) and obese men, with (n=11) or without (n=18) type 2 diabetes (HbA1c < or  $\geq$  6.5%). Underlying molecular mechanisms were examined by looking at functional receptors in the NP signalling pathway at the mRNA and protein level. Maximal ANP- and catecholamine-induced lipolysis in SCAT was blunted in obese type 2 diabetics compared with age-matched lean men whereas non-diabetic obese subjects showed intermediate responses. This blunted ANP-mediated lipolytic response was accompanied by lower mRNA and protein expression of the type-A natriuretic peptide (NP) receptor and higher mRNA but reduced protein expression of the scavenging type-C receptor. Maximal ANP-induced lipolysis was lower in VAT compared with SCAT but not different between groups. Collectively, our data show that both ANP- and catecholamine-mediated lipolysis is attenuated in SCAT of obese men with type 2 diabetes, and might be partially explained by NP receptor defects. Therefore, improving maximal ANP responsiveness in adipose tissue might be a potential novel strategy to improve obesity-associated metabolic complications.